## Discovering Cell Mechanisms

oxidase, NADH cytochrome c reductase, NADPH cytochrome c reductase, and fumarase. Although the cytochrome c reductases and fumarase did not, acid ribonuclease, acid deoxyribonuclease, cathepsin all fractionated with acid phosphatase and  $\beta$ -glucuronidase. Each of the enzymes that fractionated together functions, in conjunction with water, to degrade a macromolecule into its subunits through a reaction that follows the formula

$$AB + H_2O \rightarrow AH + BOH$$
.

The hydrolytic nature of these enzymes led de Duve to propose the name *lysosome* (from the Greek work *lusis*, meaning to untie) for this component (de Duve et al., 1955).<sup>43</sup> He also proposed that there was a good reason why this group of enzymes might co-occur in a separate organelle: otherwise they would interfere with synthetic processes and disrupt cell structure. Urate oxidase had a similar distribution as the lysosome enzymes but showed no latency and was not brought into solution by the same treatments as sufficed for the hydrolases. In subsequent research, he identified it as a constituent of yet another organelle, the peroxisome.<sup>44</sup>

In conjunction with the Third International Congress of Biochemistry in Louvain in 1955 Alex Novikoff visited de Duve's laboratory for six weeks. Novikoff took samples of de Duve's lysosome preparation to Claude's laboratory in Brussels and then to Bernhard's laboratory in Paris to examine them with the electron microscope. The micrographs revealed particles<sup>45</sup> that had occasionally been seen in electron micrographs a year earlier by Charles Rouillier, who had named them "pericanalicular dense bodies" because they were structures impenetrable to electrons found along bile canaliculi. Novikoff described these structures as having a mean length of 0.37µ and as

<sup>&</sup>lt;sup>43</sup> The choice of name was explained by de Duve (1969, p. 14): "Lysosome sounded too much like lysozyme; lysosome could be confused with lyo-enzyme, which already had a meaning; hydrosome brought to mind the image of some marine contraption. We finally settled for lysosome, well aware of the danger of our choice." By the early 1960s a total of twelve enyzmes were associated with the lysosome, each capable of splitting important biological compounds in a slightly acid environment: acid phosphatase, cathepsin A and B, acid desoxyribonuclease, acid ribonuclease, β-glucuronidase, arhylsulfatase A and B, phosphoprotein phosphatase, β-galactosidase, β-N-acetylglucosamidase, and α-mannosidase (Novikoff, 1961). By 1980 the number had grown to thirty-six.

<sup>&</sup>lt;sup>44</sup> In these investigations, de Duve found that urate oxidase segregated with three additional enzymes, two of which were involved in the synthesis of hydrogen peroxide (d-amino acid oxidase and α-hydroxyl acid oxidase) and one in its breakdown (catalase). He linked all four enzymes to the peroxisome, which he identified with what had previously been referred to as *microbodies*.

<sup>&</sup>lt;sup>45</sup> His experience of seeing the micrographs was described by de Duve (1969, p. 16) as "like Le Verrier after the planet Neptune was discovered."